Office Action Summary	Application No.	Applicant(s)	
	10/595,895	KREPSKI ET AL.	
	Examiner	Art Unit	
	Rita J. Desai	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-78* is/are pending in the application.

4a) Of the above claim(s) *29-31 and 74-78* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-28,32-73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/1/06*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *6/25/09* .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The previous examiner had made a restriction and had included the method along with the compounds.

The examiner is further restricting and has made new groups.

Election/Restrictions

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I claim(s) 2-28, 32-73 drawn to compounds and compositions wherein Ra and Rb form a six membered carbocyclic ring.

Group II, claim(s) 2-28, 32-73 drawn to compounds and compositions wherein Ra and Rb form a six membered one N containing heterocyclic ring.

Group III, claim(s) 2-28, 32-73 drawn to compounds and compositions wherein Ra and Rb do not form a ring.

Group IV, claim(s) 2-28, 32-73 drawn to compounds and compositions wherein Ra and Rb is other than in groups I-III.

Group V-IX, claim(s) 29-31, 74-78, drawn to a method of treating limited to the scope of the compounds of one of the groups I to IV.

The inventions listed as Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:
(f) •Markush Practice.• The situation involving the so-called •Markush practice• wherein a single claim defines alternatives (chemical or non-chemical) is also governed by Rule 13.2. In this special situation, the requirement of a technical interrelationship and the same or

corresponding special technical features as defined in Rule 13.2, shall be considered to be met when the alternatives are of a similar nature.

(i) When the Markush grouping is for alternatives of chemical compounds, they shall be regarded as being of a similar nature where the following criteria are fulfilled:

(A) all alternatives have a common property or activity, and

(B)(1) a common structure is present, i.e., a significant structural element is shared by all of the alternatives, or

(B)(2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains.

(ii) In paragraph (f)(i)(B)(1), above, the words •significant structural element is shared by all of the alternatives• refer to cases where the compounds share a common chemical structure which occupies a large portion of their structures, or in case the compounds have in common only a small portion of their structures, the commonly shared structure constitutes a structurally distinctive portion in view of the existing prior art. The structural element may be a single component or a combination of individual components linked to-gether.

The different Ra, Rb and the various substituents have so many variables with the heterocyclic and non-hetero groupings , they have different bonding and properties , and have achieved a different status in the art , and is burdensome to search and hence are objected to as being drawn to an improper Markush group on the grounds of lack of a common nucleus. The terms Ra, Rb and the various substituents are so broad in scope that a prior art reference anticipating the claims with respect to one member under 35 USC 102(b) would not render obvious the same claims under 35 USC 103a with respect to another member.

Also see US 6573273 claims and also US 6656938 Crooks et al , claims which indicates that the core is not novel and not a contribution over the prior art.

During a telephone conversation with Mr Hunter Baker on 6/25/09 a provisional election was made with traverse to prosecute the invention of Group I, claims as the species for search purposes. The claims encompassing the elected species include claims 2, 3, 4, 12, 13, 14, 18, 19, 20, 21, 22, 24, 25, 26, 27, 28, 41, 42, 43, 44, 45, 47, 48, 49, 71, 72, 73.

Affirmation of this election must be made by applicant in replying to this Office action.

Claims drawn to groups II to IX are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

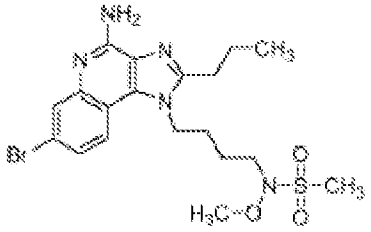
Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the

currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

The applicants have further elected the species of formula



Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-4, 12, 13, 14, 18-22, 24-28, 41-45, 47-49, 71-73 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for R' to be alkyl or alkoxy and X to be an alkyl , and R1-2, R1-3 are an alkyl or alkyl substituted by a phenyl or pyridine, does not reasonably provide enablement for the pages and pages of substituents as given. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or

use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

1) The breadth of the claims: The instant claims encompass many compounds . The scope with the various permutations and combinations is huge.

hydrogen,

alkyl,

aryl,

alkylene-aryl,

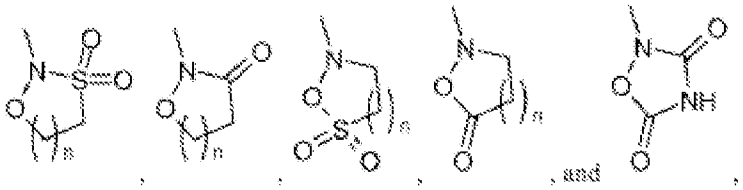
heteroaryl,

alkylene-heteroaryl, and

alkyl, aryl, alkylene-aryl, heteroaryl, or alkylene-heteroaryl substituted by one or more substituents selected from the group consisting of:

alkoxy,
dialkylamino,
-S(O)$_{0-2}$-alkyl,
-S(O)$_{0-2}$-aryl,
-NH-S(O)$_2$-alkyl,
-NH-S(O)$_2$-aryl,
haloalkoxy,
halogen,
cyano,
nitro,
aryl,
heteroaryl,
heterocyclyl,
aryloxy,
arylalkyleneoxy,
-C(O)-O-alkyl,
-C(O)-N(R_8)$_2$,
-N(R_8)-C(O)-alkyl,
-O-(CO)-alkyl, and
-C(O)-alkyl;

or the R_{1-2} and R_{1-3} groups can join together to form a ring system selected from the group consisting of:



wherein n = 0, 1, 2, or 3;

R_{1-3} is selected from the group consisting of:

alkyl,
aryl,

and so on for pages.

2) The nature of the invention: The invention is a (highly) substituted tricyclic compound for pharmaceutical use.

3) The state of the prior art: Several similar tricyclic compounds are known but not with the numerous substitutions as given by the specifications.
4) The level of one of ordinary skill: The ordinary artisan is highly skilled.

5) The level of predictability in the art: It is noted that the pharmaceutical art is unpredictable , requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statue. The level of unpredictability is in the art is very high. The compounds which differ by a methyl group also show different properties, for e.g. theophylline and caffeine. One of them is a bronchodilator and they differ only by a methyl group.
Also it is not easy to synthesize organic compounds.
As stated in the preface to a recent treatise:

"Most non-chemists would probably be horrified if they wereto learn how many attempted syntheses fail, and how inefficient research chemists are. The ratio of successful to unsuccessful chemical experiments in a normal research laboratory is far below unity, and synthetic research chemists, in the same way as most scientists, spend most of their time working out what went wrong, and why. Despite the many pitfalls lurking in organic synthesis, most organic chemistry textbooks and research articles do give the impression that organic reactions just proceed smoothly and that the total synthesis of complex natural products, for instance, is maybe a labor-intensive but otherwise undemanding task. In fact, most syntheses of structurally complex natural products are the result of several years of hard work by a team of chemists, with almost every step requiring careful optimization. The final synthesis usually looks quite different from that originally planned, because of unexpected difficulties encountered in the initially chosen synthetic sequence. Only the seasoned practitioner who has experienced for himself the many failures and frustrations which the development (sometimes even the repetition) of a synthesis usually implies will be able to appraise such work .....Chemists tend not to publish negative

results, because these are, as opposed to positive results, never definite (and far too copious)

....." Dorwald F. A.

Side Reactions in Organic Synthesis, 2005, Wiley: VCH, Weinheim pg. IX of Preface.

6) The amount of direction provided by the inventor: The inventor provides very little direction in the instant specification. There are only limited examples and it does not commensurate to the scope of the claims.

7) The existence of working examples: The instant specification has only few examples and no data to show that these did have any pharmaceutical activity.

8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: Since there are no working examples, the amount of experimentation is very high and burdensome.

Taking the above eight factors into consideration, it is not seen where the instant specification enables the ordinary artisan to make and/or use the instantly claimed invention.

Genetech Inc Vs Nova Nordisk 42 USPQ 2d 1001.

"A patent is not a hunting license. It is not a reward for search but compensation for its successful conclusion and patent protection is granted in return for an enabling disclosure of an invention , not for vague intimations of general ideas that may or may not be workable."

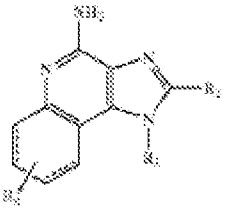
MPEP 2164.01(a) states, "A conclusion of lack of enablement means that,

based on the evidence regarding each of the above factors, the specification, at the time the application was flied, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed.

Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

Claims 2-28,32-73 are rejected under 35 U.S.C. 102(b) as being anticipated by US 6573273 Crookes et al

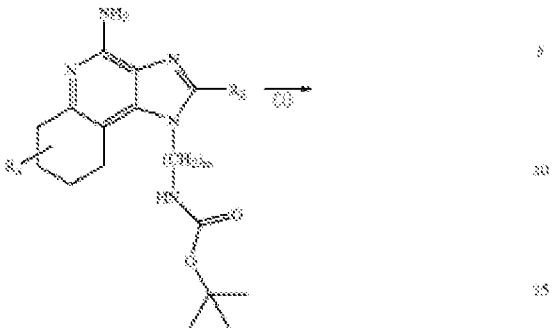
The reference discloses compounds of the formula



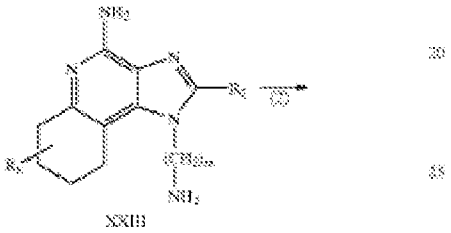
wherein

R_3 is -alkyl-NR_5—CO—O—R_4 or -alkenyl-NR_5—CO—O—R_4;

R_4 is aryl, heteroaryl, heterocyclyl, alkyl or alkenyl, each of which may be unsubstituted or substituted by one or more substituents selected from the group consisting of:



XXII



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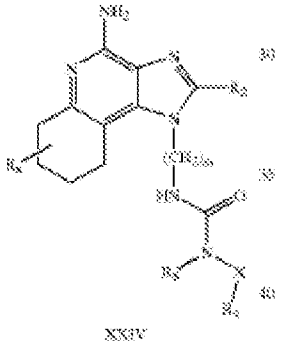

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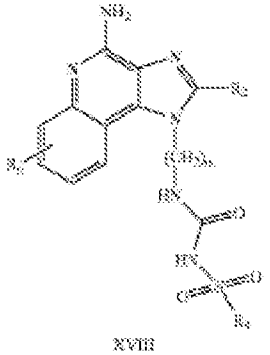
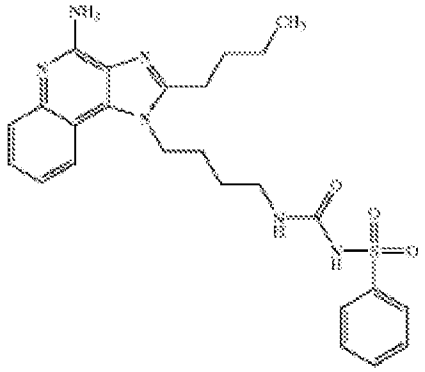


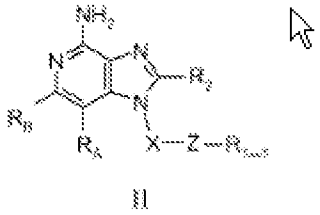
XVIII



Claims 2-28, 32-73 rejected under 35 U.S.C. 102 as being anticipated by Crooks US 6656938.,

The prior art discloses compounds such as

The instant invention is also drawn to similar compound.



II

where in X is an alkyl chain interrupted by an O, Z is an oxime or an urea group and R2 is an alkyl group, and Ra and Rb together form a carbocyclic ring.

Claim Rejections - 35 USC § 103

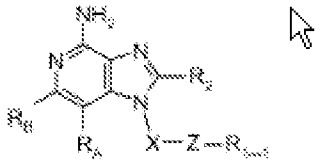
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2-28, 32-73are rejected under 37 USC 103 as being unpatentable over Crooks et al US 6573273 and Us 6656938.

Applicants claims are drawn to compounds of the formula



II

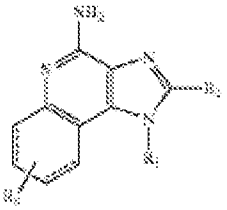
where in X is an alkyl chain interrupted by an O, Z is an oxime or an urea group and R2 is an alkyl group, and Ra and Rb together form a carbocyclic ring.

Scope & Content of Prior Art MPEP 2141.01

The prior art teaches similar compounds.

The reference discloses compounds of the formula

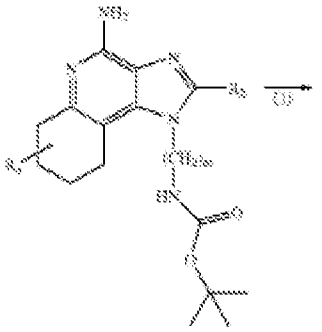
(Ic)



wherein

R_2 is -alkyl-NR_3---CO---O---R_4 or -alkenyl-NR_3---CO---O---R_4;

R_4 is aryl, heteroaryl, heterocyclyl, alkyl or alkenyl, each of which may be unsubstituted or substituted by one or more substituents selected from the group consisting of.



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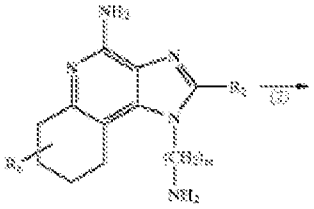

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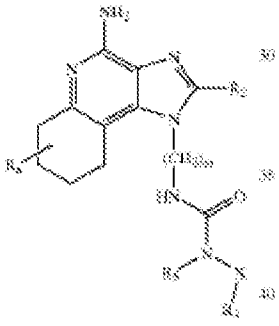
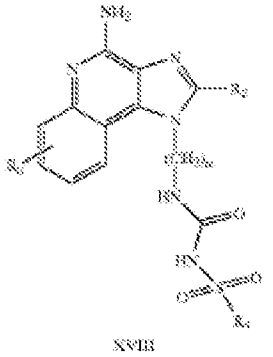
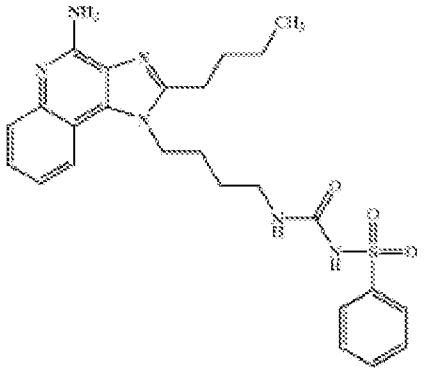


XXIV



XVIII



Difference between Prior Art and the claims MPEP 2141.02

The generic compounds are disclosed with the various options.

Prima Facie Obviousness , Rational and Motivation MPEP 2142-2413

Sinve many substitutions and variables are disclosed in the prior art and knowing that similar compounds have similar activity, one of skill in the art would be motivated to make various variations on the X, R1 to obtain the compounds of the invention. The specifications do not have any showing of unexpected results, thus in the absence of unexpected results the claims are obvious over the prior art.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 2-28, 32-73 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 12/092625, claim 1 of 11/885006, claim 1 of 11/885005, 11/595790(positional isomers), 11/570716 (claim 3), 10/595065, 10/595792. Although the conflicting claims are not identical, they are not patentably distinct from each other because they have a similar core with the same oxime substituent and they are also drawn to the same use. The current application is devoid of a showing of any unexpected results.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita J. Desai whose telephone number is 571-272-0684. The examiner can normally be reached on Monday - Friday, flex time..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Rita J. Desai/
Primary Examiner, Art Unit 1625

June 26th, 2009.